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Water Percolation Governs Polymorphic Transition and Conductivity of DNA

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We report on the simulation studies of the percolation transition of water at the surface of the DNA double helix. At low hydrations, only small water clusters are attached to the DNA surface, whereas it is homogeneously covered by a spanning water network at high hydrations. Formation of a spanning water network occurs via a percolation transition at the hydration level close to the midpoint of polymorphic transition between A- and B-forms of DNA. This percolation transition results in sigmoid like acceleration of long-range ion transport in good agreement with experiment.

The presence of water at the surface of biomolecules is necessary for their conformational stability and functions. Dynamics and functions of biomolecules are often completely restored, when they are covered by about a monolayer of hydration water[1,2]. Formation of such monolayer occurs via quasi-2D percolation transition between two essentially different states of hydration water: ensemble of finite clusters and spanning hydrogen-bonded (HB) network of hydration water, which homogeneously envelopes a biomolecule[3,4]. The microscopic origin of the relationship between the percolation of hydration water and biological functions is unclear. One may expect that the appearance of a spanning network of hydration water strongly affects the dynamic properties of the hydrated biomolecule and the charge transport along the biological surfaces.

Water is crucial for the biological functions of the double helical DNA[5]. Experiments show that there is a strict relationship between the state of DNA and a hydration number Γ, measured as the number of water molecules per nucleotide. Biologically relevant B-DNA becomes unstable at hydrations $\Gamma < 20$ and midpoint of the transition between A- and B-forms of DNA is about $\Gamma = 15$.[5] In the same hydration range, conductivity DNA shows sigmoid like dependence on Γ.[6] To clarify the possible role of water percolation in the polymorphic transitions of DNA, we performed computer simulations of a rigid, dodecamer fragment of double helical DNA (CGCGAATTCGCG), fixed in space in canonical B-form, in the range of hydrations $12 \leq \Gamma \leq 30$.[7,8] The Cornell *et. al.* force field[9] was used for DNA and water was modeled by TIP3P potential.[10] The molecular dynamics (MD) simulations were carried out with the internal coordinate MD method adopted for DNA[11] with a time step of 0.01 ps. The standard duration of production runs was 10 ns with the coordinates saved every 1 ps. The clustering and percolation of water were analyzed by methods earlier developed in our group.[3,4,12–14]

The probability distribution $P(S_{max})$ of the size S_{max} of the largest water cluster on the B-DNA surface under different hydration levels is shown in Figure 1.A. The two peaks

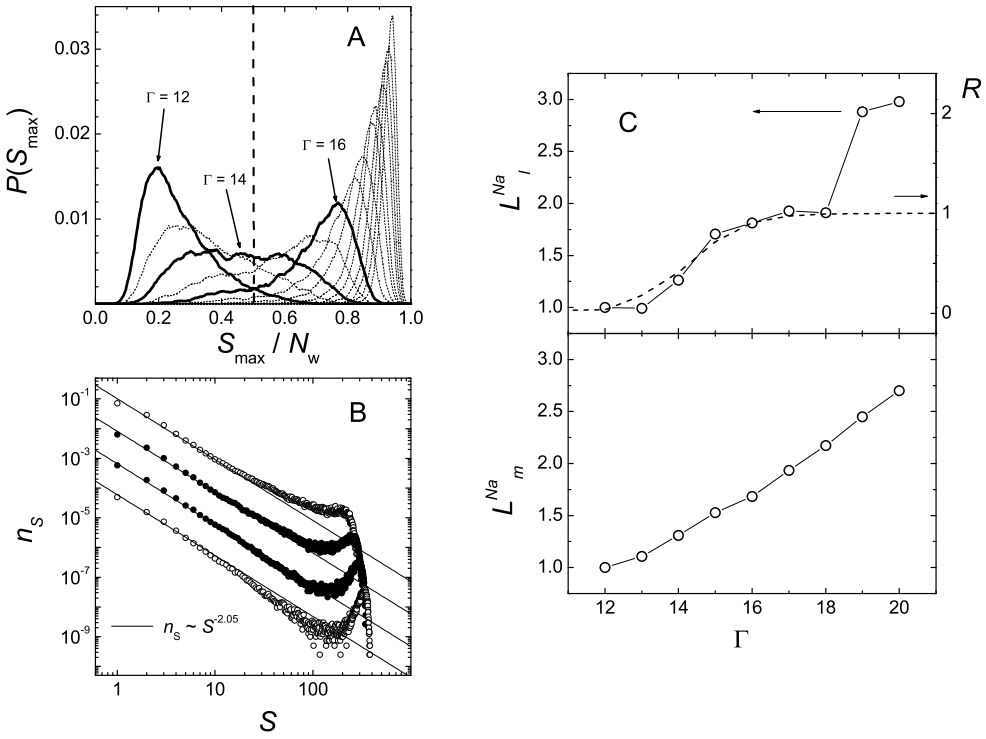

Figure 1. **A**: Probability distribution $P(S)_{max}$ of the size S_{max} of the largest water cluster on DNA surface with hydration levels Γ from 10 to 24. **B**: Distribution n_S of the size of water clusters at the surface of DNA molecule for representative hydration levels Γ from 14 (top) to 17 (bottom). The universal power law expected for 2D percolation transition is shown by solid lines. **C**: *Upper panel*: Relative mobility L_l^{Na} of ions, in time interval 200 ps $\leq$ t $\leq$ 500 ps (open circles, left axis), and percolation probability *R* of hydration water (dashed line, right axis) as function of the hydration level Γ. *Lower panel*: Dependence of the relative mobility L_m^{Na} of ions, in time interval 50 ps $\leq$ t $\leq$ 100 ps, on the hydration level Γ.

at small and large S_{max} corresponds to non-spanning and spanning HB networks, respectively. The most symmetric distribution $P(S_{max})$ is observed at a hydration level where spanning and non-spanning states of the largest cluster are equally populated, and this hydration corresponds to the midpoint of the percolation transition. The spanning probability $R(\Gamma)$ estimated from these distributions[7] is shown by dashed line in Figure 1.C (upper panel, right axes). The midpoint of the percolation transition, that is the position of the inflection point of $R(\Gamma)$ being fitted to sigmoid function, is close to $\Gamma \approx 14.3$. The true percolation threshold can be located by using the cluster size distribution n_S, which is a probability to find a cluster, containing *S* molecules. At the true percolation threshold, $n_S \sim S^{-2.05}$ in the widest range of *S*. HB water clusters at DNA surface follows this universal power law in the widest range of *S* at hydration levels $\Gamma \approx 15$ and 16 (closed symbols in Figure 1.B) and the true percolation threshold of water occurs at $\Gamma = 15.5 \pm 0.5$. At the threshold hydration, the minor groove of B-DNA is already filled with water, and the percolation transition results in formation of a spanning water network in the major

groove. The threshold hydration is strikingly close to the midpoint of the low hydration transition of DNA from the B-form to other forms.[5] This observation suggests that water percolation may be responsible for the low hydration polymorphism of DNA. So, DNA exists in biologically relevant B-form only when it is covered by a spanning water network.

To explore effect of water percolation on the mobility of Na^+ ions in the DNA hydration shell, we have analyzed time dependence of their mean square displacements $\left\langle \Delta r^2 \right\rangle (t)$. Due to confinement effect and due to heterogeneity of the DNA surface, such dependence is non-linear. We characterized ions diffusion by a dimensionless relative mobility $L(\Gamma)$ obtained as the slope of the linear fit of $\left\langle \Delta r^2 \right\rangle (t)$ in a given time interval normalized by the corresponding slope for $\Gamma = 12$. Mobility $L_m^{Na}(\Gamma)$ of Na^+ ions approximately linearly grows with hydration for short-time translations, $t \leq 100$ps (Figure 1.C, lower panel), but the relative mobility L_l^{Na}, evaluated in the time period 200 ps $\leq$ t $\leq$ 500 ps (Figure 1.C, upper panel), corresponding to the ion displacement up to 6.5 Å, behaves radically different. From hydration Γ = 12 up to Γ = 18, L_l^{Na} exhibits a sigmoid like dependence closely following the spanning probability $R(\Gamma)$. The overall increase of L_l^{Na} on passing the percolation threshold is about 100%. The step like increase of ion mobility at Γ = 18 may be attributed to the escape of ions from the DNA surface. Two step increase of the L_l^{Na} with hydration in our simulations remarkably agrees with the experimentally observed dependence of the radiation-induced conductivity of hydrated DNA fibers.[6] Ability of the spanning network of hydration water to provide ion transport along bio-surfaces may explain its crucial role in biological function.

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